

Application No. 10/612,497  
Second Supplemental Reply to a March 15, 2005 Office Action  
Second Supplemental Reply Dated June 24, 2005

**Amendments to the Claims:**

Please amend claims 116, 122, 127, 133, 137, 148, 154, 157, 163, 164, 171, 172 and 176 and add claims 231-235. This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

1.-115. (Cancelled)

116. (Currently amended) A method for ~~producing~~ expressing and recovering a human monoclonal antibody that competes for binding to CTLA-4 with an antibody comprising the heavy chain CDR amino acid sequences in SEQ ID NO: 1 and the light chain CDR amino acid sequences in SEQ ID NO: 14, wherein said competing human monoclonal antibody inhibits binding of human CTLA-4 to human B7-1 and human B7-2 and wherein said competing human monoclonal antibody comprises a light chain amino acid sequence that utilizes a human A27 V $\kappa$  gene, said method comprising the steps of:

- (a) ~~expressing said competing human monoclonal antibody in~~ culturing a mammalian host cell comprising polynucleotides encoding the heavy and light chains of said competing human monoclonal antibody; and
- (b) recovering said competing antibody.

Application No. 10/612,497  
Second Supplemental Reply to a March 15, 2005 Office Action  
Second Supplemental Reply Dated June 24, 2005

117. (Previously presented) The method according to claim 116, wherein said competing antibody inhibits binding of human CTLA-4 to human B7-1 or human B7-2 with an  $IC_{50}$  of 100 nM or less.

118. (Previously presented) The method according to claim 116, wherein said competing antibody inhibits binding of human CTLA-4 to human B7-1 with an  $IC_{50}$  of 5 nM or less.

119. (Previously presented) The method according to claim 116, wherein said competing antibody inhibits binding of human CTLA-4 to human B7-1 with an  $IC_{50}$  of 2 nM or less.

120. (Previously presented) The method according to claim 116, wherein said competing antibody inhibits binding of human CTLA-4 to human B7-2 with an  $IC_{50}$  of 5 nM or less.

121. (Previously presented) The method according to claim 116, wherein said competing antibody inhibits binding of human CTLA-4 to human B7-2 with an  $IC_{50}$  of 2 nM or less.

122. (Currently amended) The method according to claim 116, wherein a glutamine synthetase expression system is employed for the expression of said competing human monoclonal antibody ~~in said step of expressing said competing antibody.~~

Application No. 10/612,497  
Second Supplemental Reply to a March 15, 2005 Office Action  
Second Supplemental Reply Dated June 24, 2005

123. (Previously presented) The method according to claim 116, wherein said mammalian cell is a CHO cell.

124. (Previously presented) The method according to claim 116, wherein said mammalian cell is an NSO cell.

125. (Cancelled)

126. (Previously presented) The method according to claim 116, wherein said polynucleotides encode the heavy and light chain CDRs of a competing antibody that was generated in a mouse whose genome comprises human immunoglobulin genes.

127. (Currently amended) A method for ~~producing~~ expressing and recovering a human monoclonal antibody that competes for binding to CTLA-4 with an antibody comprising the heavy chain variable region amino acid sequence in SEQ ID-NO: 1 and the light chain variable region amino acid sequence in SEQ ID NO: 14, wherein said competing human monoclonal antibody inhibits binding of human CTLA-4 to human B7-1 and human B7-2 and wherein said competing human monoclonal antibody comprises a light chain amino acid sequence that utilizes a human A27 V<sub>K</sub> gene, said method comprising the steps of:

(a) ~~expressing said competing human monoclonal antibody in~~ culturing a mammalian host cell comprising polynucleotides encoding the heavy and light chains of said competing human monoclonal antibody; and

Application No. 10/612,497  
Second Supplemental Reply to a March 15, 2005 Office Action  
Second Supplemental Reply Dated June 24, 2005

(b) recovering said competing antibody.

128. (Previously presented) The method according to claim 127, wherein said competing antibody inhibits binding of human CTLA-4 to human B7-1 or human B7-2 with an  $IC_{50}$  of 100 nM or less.

129. (Previously presented) The method according to claim 127, wherein said competing antibody inhibits binding of human CTLA-4 to human B7-1 with an  $IC_{50}$  of 5 nM or less.

130. (Previously presented) The method according to claim 127, wherein said competing antibody inhibits binding of human CTLA-4 to human B7-1 with an  $IC_{50}$  of 2 nM or less.

131. (Previously presented) The method according to claim 127, wherein said competing antibody inhibits binding of human CTLA-4 to human B7-2 with an  $IC_{50}$  of 5 nM or less.

132. (Previously presented) The method according to claim 127, wherein said competing antibody inhibits binding of human CTLA-4 to human B7-2 with an  $IC_{50}$  of 2 nM or less.

133. (Currently amended) The method according to claim 127, wherein a glutamine synthetase expression system is employed in said step of ~~expressing said competing~~